

CLAIMS:

1. A cyclic compound comprising one or more cyclic  
moieties, which has a biological activity of brain-derived  
5 neurotrophic factor (BDNF).

2. A compound according to claim 1, wherein the  
compound is monocyclic monomeric, bicyclic dimeric, or  
tricyclic dimeric, as described herein.

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3. A compound according to claim 2, wherein the  
compound is a bicyclic dimeric compound of general formula  
(I):



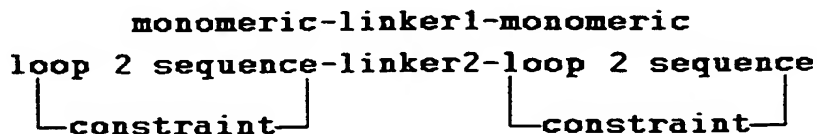
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(I).

4. A compound according to claim 3, wherein the  
constraint comprises a covalent grouping of atoms.

20 5. A compound according to claim 4, wherein the  
constraint and the linker may be the same or different.

6. A compound according to claim 2, wherein said  
compound is a tricyclic dimeric compound of general formula  
25 (II):



(II).

7. A compound according to claim 6, wherein each of  
30 the constraint, linker 1 and linker 2 may be the same or

different.

8. A compound according to any one of claims 3 to 7,  
wherein each of the constraint, linker, linker 1 or linker  
5 2 has between at 0 to 20 carbon atoms, and 0 to 10  
heteroatoms, wherein said heteroatoms are selected from the  
group consisting of N, O, S, and P.

9. A compound according to claim 8, wherein each of  
10 the constraint, linker, linker 1 or linker 2, is either a  
straight or branched chain containing either saturated,  
unsaturated and/or aromatic rings.

10. A compound according to claim 8 or claim 9,  
15 wherein each of the constraint, linker, linker 1 or linker  
2, comprises single and/or double bonds.

11. A compound according to according to any one of  
claims 8 to 10, wherein each of the constraint, linker,  
20 linker 1 or linker 2, comprises one or more chemical groups  
selected from the group consisting of amide, ester,  
disulphide, thioether, ether, phosphate and amine.

12. A compound according to any one of claims 3 to  
25 10, wherein the constraint is obtained by either:

(i) cyclising the N-terminal amine with the C-  
terminal carboxyl acid function, either directly via an  
amide bond between the N-terminal nitrogen and C-terminal  
carbonyl, or indirectly via a spacer group; or

30 (ii) cyclising via the formation of a covalent  
bond between the side chains of two residues, either  
directly or via a spacer group as described in (i) above ;  
or

(iii) a disulphide bond between two cysteine  
35 residues, either directly or via a spacer group as  
described in (i) above; or

(iv) a thioether bond between a cysteine residue

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and an  $\omega$ -halogenated amino acid residue, either directly or via a spacer group as described in (i) above; or

- (v) cyclising via the formation of an amide bond between a side chain and either the C-terminal carboxyl or N-terminal amine, either directly or via a spacer group as described in (i) above.

13. A compound according to any one of claims 3 to 10, wherein each of the linker, linker 1 or linker 2 is obtained by either:

- (i) cyclising via the formation of a covalent bond between the side chains of two residues, either directly or via a spacer group; or
- (ii) a disulphide bond between two cysteine residues, either directly or via a spacer group as described in (i) above; or
- (iii) a thioether bond between a cysteine residue and an  $\omega$ -halogenated amino acid residue, either directly or via a spacer group as described in (i) above; or
- (iv) cyclising via the formation of an amide bond between a side chain and either the C-terminal carboxyl or N-terminal amine, either directly or via a spacer group as described in (i) above.

14. A compound according to claim 12 or claim 13, wherein said formation of a covalent bond between the side chains of two residues is via the formation of an amide bond between a lysine residue and either an aspartic acid or glutamic acid residue.

15. A compound according to claim 12 or claim 13, wherein the side chain in (ii) is either a lysine or an aspartate residue.

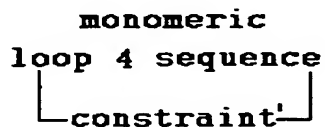
16. A compound according to claim 12, wherein the cyclising of the N-terminal amine with the C-terminal carboxyl acid is via condensation with an  $\omega$ -amino

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carboxylic acid.

17. A compound according to any one of claims 12 to 16, wherein the residues contributing to the side chains  
5 are either derived from the monomeric loop 2 sequence itself, or incorporated into or added on to the monomeric loop 2 sequence.

18. A compound according to claim 2, wherein said  
10 compound is a monomeric, monocyclic compound of general formula (III):



(III).

19. A compound according to claim 17, wherein said  
15 constraint is obtained by cyclising the N-terminal amine with the C-terminal carboxyl acid function, either directly via an amide bond between the N-terminal nitrogen and C-terminal carbonyl, or indirectly via a spacer group.

20. A compound according to claim 19, wherein the  
20 spacer group consists of one or more additional amino acid residues.

21. A compound according to claim 20, wherein the one  
25 or more additional amino acid residues includes  $\alpha$ - and  $\omega$ -amino carboxylic acid residues.

22. A compound according to claim 20, wherein the  
30 residues contributing the side chains are derived from the monomeric loop 4 sequence itself, or incorporated into or added on to the monomeric loop 4 sequence.

23. A compound according to any one of claims 1 to 22, wherein one or more amino acids is replaced by its

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corresponding D-amino acid.

24. A compound according to any one of claims 1 to 23, wherein one or more peptide bonds is replaced by a structure more resistant to metabolic degradation.

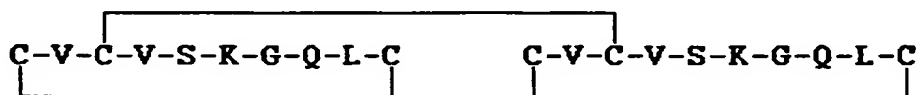
25. A compound according to any one of claims 1 to 23, wherein individual amino acids in said compound are replaced by analogous structures as described herein.

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26. A compound according to claim 25, wherein said analogous structures are selected from the group consisting of *gem*-diaminoalkyl groups, alkylmalonyl groups (with or without modified termini), alkyl, acyl and amine groups.

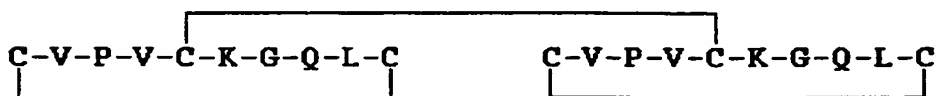
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27. A compound according to claim 1, wherein said compound is of formula (IV) or formula (V):



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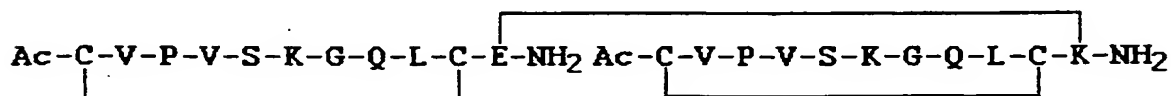
(IV)



(V).

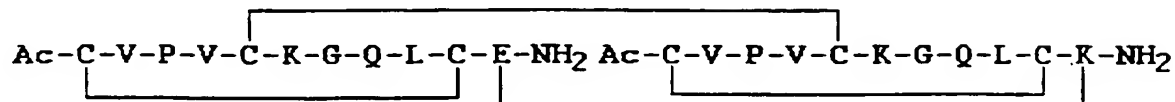
28. A compound according to claim 1 wherein said compound is of formula (VI):

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(VI).

29. A compound according to claim 1, wherein said compound is of formula (VII):



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(VII).

30. A compound according to claim 1, wherein said compound is of formula (VIII):

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(VIII).

31. A composition, comprising a compound according to any one claims 1 to 30, together with a pharmaceutically-acceptable carrier, or a carrier or diluent which does not adversely affect the growth of cells in culture.

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32. A composition according to claim 30, wherein said composition is formulated for oral, intravenous, subcutaneous, intramuscular, intrathecal, intraventricular or topical administration.

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33. A composition according to claim 31 or claim 32, wherein the carrier is selected from the group consisting of dextrose, mannitol, sucrose, and lactose.

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34. A composition according to claim 33, further comprising one or more buffer and/or bulking agents.

30

35. A composition according to claim 34, wherein the buffer is selected from the group consisting of acetate,

citrat and phosphate.

36. A composition according to claim 34, wherein the bulking agent is selected from the group consisting of  
5 serum albumin and human serum albumin.

37. A composition according to claim 31, used as a culture medium additive for promotion of growth of neuronal cells *in vitro*.  
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38. A composition according to claim 37, wherein the carrier or diluent is water, a saline solution, or a buffer solution.

15 39. A composition according to claim 37 or claim 38, wherein the concentration of compound is in the range 1-500µM.

40. A culture medium according to claim 39, wherein  
20 the concentration of compound is in the range 1-100µM.

41. A method of treating a condition characterised by neuronal deficit or neuronal death, comprising the step of administering an effective amount of a compound according to  
25 to any one of claims 1 to 30, or a composition according to any one of claims 31 to 37, to a subject in need of such treatment.

42. A method according to claim 41, wherein the  
30 condition being treated is selected from the group consisting of neurodegenerative diseases, neurodegenerative conditions caused by insult, and peripheral sensory neuropathies.

35 43. A method according to claim 42, wherein the neurodegenerative diseases are selected from the group consisting of motor neurone disease (amyotrophic lateral

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sclerosis), progressive spinal muscular atrophy, infantile muscular atrophy, Charcot-Marie-Tooth disease, Parkinson's Disease, Parkinson-Plus syndrome, Guamanian Parkinsonian dementia complex, progressive bulbar atrophy and  
5 Alzheimer's disease.

44. A method according to claim 42, wherein the insult arises from ischaemia, hypoxia, neural injury, surgery, and exposure to neurotoxins such as N-methyl-4-  
10 phenyl-1,2,3,6-tetrahydropyridine).

45. A method according to claim 42, wherein the peripheral sensory neuropathies result from exposure to drugs (such as cis-platin), toxins, diabetes and  
15 mononeuropathy multiplex.

46. A method according to claim 41, wherein the route of administration is selected from the group consisting of oral, intravenous, subcutaneous, intramuscular,  
20 intrathecal, intraventricular and topical.

47. Use of a compound according to any one of claims 1 to 30, or a composition according to any one of claims 31 to 37 in the manufacture of a medicament used for treating  
25 a condition characterised by neuronal deficit or neuronal death.

48. Use according to claim 47, wherein the condition being treated is selected from the group consisting of  
30 neurodegenerative diseases, neurodegenerative conditions caused by insult, and peripheral sensory neuropathies.

49. Use according to claim 48, wherein the neurodegenerative diseases are selected from the group  
35 consisting of motor neurone disease (amyotrophic lateral sclerosis), progressive spinal muscular atrophy, infantile muscular atrophy, Charcot-Marie-Tooth disease, Parkinson's



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Disease, Parkinson-Plus syndrome, Guamanian Parkinsonian dementia complex, progressive bulbar atrophy and Alzheimer's disease.

- 5    50.            Use according to claim 48, wherein the insult arises from ischaemia, hypoxia, neural injury, surgery, and exposure to neurotoxins such as N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine).
- 10   51.            Use according to claim 48, wherein the peripheral sensory neuropathies result from exposure to drugs (such as cis-platin), toxins, diabetes and mononeuropathy multiplex.
- 15   52.            Use according to claim 47, wherein the route of administration is selected from the group consisting of oral, intravenous, subcutaneous, intramuscular, intrathecal, intraventricular and topical.